SMMGP Clinical Update - August 2010

Survival of hepatitis C virus in syringes: implication for transmission among injection users. *Paintsil E, Huije H, Peters C, et al. The Journal of Infectious Diseases 2010; 202(7): 1 October*

This study hypothesized that the high prevalence of hepatitis C virus (HCV) among injecting drug users might be due to prolonged virus survival in contaminated syringes.

The residual volume (void volume) that remains in a syringe after injection depends on the size and the design of the syringe. Generally, syringes with a fixed needle have a low residual volume while syringes with detachable needles tend to retain fluid in the hub of the syringe as well as the base of the plunger and needle. Therefore, they usually have a high residual volume.

This study looked at low-void and high-void syringes. They developed a micro-culture assay that measured HCV. They then introduced blood with HCV into the syringes and emptied them again. They stored them at 4˚C, 22˚C and 37˚C for up to 63 days before testing for HCV infectivity.

The insulin syringes (the low-void fixed needles) failed to yield HCV beyond day 1 at all storage temperatures except 4˚C when 1 in 20 had viable virus at day 7. In the high-void syringes virus was obtained from 96%, 71% and 52% of syringes after storage at 4˚C, 22˚C and 37˚C for 7 days. There was still viable virus up to day 63.

Hepatitis C testing, 2009 report. Analysis of 2009 and trend (2005-2009) data. *Health Protection Agency. Report 8: August 2010. Available at www.hpa.org.uk*

This is now the eighth annual HCV report from sentinel surveillance of hepatitis testing in England for 2009. This is the first year where data from dried blood spot testing was also available.

Overall, the trend of increased first line testing for hepatitis C antibodies (anti-HCV) has continued. In 2009 151,543 individuals were tested for hepatitis C antibodies at the sentinel sites. Overall, the number and proportion of individuals testing positive has continued to decline and in 2009 there were 2.7% who tested positive. Half of those tested and 60% of the positives were aged 24 to 44 years. Individuals identified as being South Asian (through name analysis software) accounted for 13% of all individuals tested and they had the same proportion of positive tests.

There was an increased risk of infection amongst female IDUs but data on IDUs was limited by incomplete data on request forms. The report also highlighted the importance of testing in primary care – the greatest number of anti-HCV positive individuals were tested by general practice.

SMMGP comment:
The first study was very much lab-based but it has clinical relevance and it drives home the importance of effective harm reduction advice. The authors point out that the estimated probability of transmission of HCV per exposure to a contaminated syringe is 5 to 20-fold higher than that for HIV transmission. They go on to speculate that the disproportionate prevalence of HCV compared with HIV could be partly explained by the differences in survival of these viruses in the syringe shown in this study. The immediate clinical relevance might be to consider asking injecting users about their needle types and encouraging them to move to fixed needles.

Some of the data in the HPA report are encouraging. A lower percentage of HCV positives suggests either a declining incidence or a wider net is now being cast to pick up HCV. We need to keep pursuing them, and more importantly, we need to make sure we are offering further investigation and treatment, where appropriate, to those who do test positive. There was some evidence that the rate of increase in testing is slowing – as the report comments this could indicate that the pool of 'easy to reach' individuals has been exhausted.

Meta-analysis of drug-related deaths soon after release from prison. *Merrall ELC, Kariminia A, Binswanger IA, et al. Addiction, 105, 1545-1554*

This meta-analysis explored the risk of death on release from prison. The study compared the deaths in weeks 1+2 as well as weeks 3+4 and compared these with later 2 week periods in the first 12 weeks after release from prison.

After the process of sifting the evidence they had six studies from six prison systems that met the inclusion criteria. The weighty numbers from these studies add up to 69093 person-years and 1033 deaths; of these 612 deaths were drug related.

The results showed a 3 to 8-fold increase in deaths in the first two weeks compared with weeks 3-12. The authors commented on the variation between countries with the increased risk ranging from 3.1 (95% CI: 1.3-2.2) in New Mexico to 8.4 (95% CI: 5.0-14.2) in the USA. The UK showed an increased risk of 7.5 (95% CI: 5.7-9.9).

Importantly, they also pooled the data for weeks 3+4 and this showed an increased risk of 1.7 (95% CI: 1.3-2.2) compared with weeks 5 to 12.

Drug use and opioid substitution treatment for prisoners. *Stöver H, Michels II. Harm Reduction Journal. 2010. http://www.harmreductionjournal.com/content/7/1/17*

This paper is a non-systematic review that compares the quality of drug treatment for inmates with people in the community. It starts by asking the obvious, but important, question about the reasons for the lack of parity between prison and community treatment. It takes a look at the benefits to the prisoner and the benefits to the prison staff and the community.

The study highlights that "coercive abstinence in prison may be followed by relapse immediately after release, often resulting in overdose, drug emergencies and death". It gives advice on some of the areas to exploit for overcoming barriers from prison staff and other stakeholders.

SMMGP comment: The meta-analysis on prison deaths confirms the increased risk of drug-related death in the first 2 weeks on release from prison. Importantly, they have also shown that the risk persists through to weeks 3 and 4, though, as one would expect, it is tapering off as time passes. The exorbitant death rate demonstrated again in this study is a timely reminder to clinicians of the real risk that prisoners, particularly newly detoxed ones, face on release.

The second paper is a neat summary of some of the issues facing clinicians concerned with opiate substation therapy in the secure environment. The recent Department of Health update to the IDTS treatment guidelines has no clinical rationale - it is a political amendment to a clinical guideline. Clinicians who find themselves being pressured to reduce or cease prescribing of opiate substitution treatment will find much in this paper to reassure and will find it helpful when arguing the case.

Can a targeted GP-led clinic improve outcomes for street sex workers who use heroin? *Litchfield J, Maronge A, Rigg T. British Journal of General Practice 2010; 60:514-516*

This paper looked at the outcomes from a primary care drugs treatment programme for street sex workers. They set up a 'one-stop shop' where sex workers in Derby could access a full range of medical, social and drug treatment services including prescribed treatments for heroin addiction, contraception and sexual health services.

They recruited 34 participants who met the inclusion criteria: female heroin users who had offered sex for money in the previous 4 weeks. They used the Christo inventory to measure quality of life in people who use drugs and measured them at entry and at one year. They self-reported on involvement in sex work and measured heroin use through the overall percentage of positive urine samples.

The results showed an improvement in health and wellbeing with the mean Christo scores reduced from 12.05 at entry to 8.97 at 1 year ($p<0.001$). Out of the 34 women at the start only 11 (33%) reported being involved in sex work at 1 year. They had 30 urine samples at the start of the study of which 26 (87%) were positive for heroin and 21 out of 29 (72%) were positive at 1 year.

Management of drug misuse: an 8-year follow-up survey of Scottish GPs.
Matheson C, Porteous T, van Teijlingen E and Bond C. British Journal of General Practice 2010; 60:517-520

This was a follow up to a nationwide survey of GPs in Scotland completed in 2000. They used a similar questionnaire and sent it to a random sample of one in four Scottish GPs (n=1065). After a poor initial response they sent an abbreviated questionnaire on the key areas from the main questionnaire.

The main questionnaire was completed by 447 GPs and the short questionnaire by a further 173 GPs giving an overall response rate of just over 60%. This represents almost 40% of all Scottish practices.

The proportion of responders currently treating drug misusers was 43.7% and this is a statistically significant decrease compared to 2000 (62.3% $p<0.001$). The most common reason for not treating drug users was given as 'practice policy' (59.3%). However, almost 45% of GPs said an enhanced service was provided by the practice. The questionnaire also enquired into methadone prescribing. The maximum dose that GPs would prescribe in 2000 was less than 60mg in 33.6% of respondents but this has dropped to 6.8% in 2008.

SMMGP comment: This pair of papers from the BJGP looks at a couple of facets of substance misuse and primary care. The Litchfield paper rightly highlights the difficulties in accessing this group of people.

It would be easy to be critical of this paper and one can highlight the relatively small numbers, the absence of controls and the fact that the only objective outcome wasn't significantly changed. However, that would rather miss the underlying point – it should be read for inspiration as much as anything. It highlights the scope of general practice to access 'hard to reach' groups, address inequality and improve health.

The survey of Scottish GPs is encouraging that GPs seem to be more comfortable prescribing at the recommended effective levels. The apparent reduction in the number of GPs treating substance users may reflect an increase in GPs with a special interest with better organisation within practices rather than an actual reduction in care delivered.

Methadone prescribing had dropped but overall the levels of opiate substitution were much the same when buprenorphine and dihydrocodeine preparations were considered. One finding the authors did not comment on was the number of practices that prescribe benzodiazepine maintenance.

While this has dropped from 45% to 32% it does seem worthy of remark that nearly one-third of users have long term benzo scripts. It is also notable that short-term community detoxification and referral to residential detoxification had dropped from levels of around 39% in 2000 to 24-25% in 2008. While this may represent service user preference it would be concerning if there were issues around access that have driven this percentage down.

Survival and cessation in injecting drug users: prospective observational study of outcomes and effect of opiate substitution therapy. *Kimber J, Copeland L, Hickman M, et al. BMJ 2010; 340: c3172*

This paper in the BMJ was a prospective cohort study based in a large primary care facility in a deprived area of Edinburgh.

They had 794 patients with a history of injecting drug use presenting to them between 1980 and 2007. The followed up 655 (82%) by either interview or linkage to primary care records and the mortality registers. Of the 655 there were 557 (85%) who had received opiate substitution therapy.

The results showed that out of the whole cohort a total of 277 participants had achieved long term cessation of injecting and 228 died. Half of the survivors had poor health related quality of life. The median duration from first injection to death was 24 years in those with HIV and 41 years for those without HIV. For each additional year of opiate substitution treatment the hazard of death before long term cessation fell 13% (95% CI: 9-17%). It was also noted that the exposure to opiate substitution therapy was inversely related to the chances of achieving long term cessation.

SMMGP comment: This paper showed that opiate substitution treatment in primary care for injecting users reduces the risk of mortality with survival benefits increasing with cumulative exposure. There is a dose-response relationship.

One of the study's interesting wrinkles is that treatment did not reduce the overall duration of injecting.

This doesn't particularly damage the case of opiate substitution therapy – after all, the health benefits were still there and it may be that the advantages are conferred through wider benefits of improved social functioning, reduced criminal activity or just the regular contact with primary care services.

The study also highlights the dire multiple adverse health consequences of injecting drug use. The top three causes of the 228 deaths were HIV (n=102), drug overdose (n=55) and liver disease (n=26).

Some may be alarmed by the continued injecting in this population, but it highlights the difficulty for anyone to achieve long-term cessation. There is very rarely a quick fix and we need to take the long view in many cases.

The authors finish by emphasising that the findings also clearly indicate that insisting on complete abstinence from injecting in order to continue opiate substitution therapy is inappropriate and likely to increase mortality.

Treatment of opioid dependence in adolescents and young adults with extended release naltrexone: preliminary case-series and feasibility. *Fishman MJ, Winstanley EL, Curran E, et al. Addiction 2010; 105: 1669-1676*

This American study looked at 16 cases of opioid dependence in adolescent and young adults (mean age 18.5 years) who had received extended-release naltrexone.

The group have been using an extended-release naltrexone preparation which has been licensed for use in the USA since 2006 for alcohol dependence. They have been using it 'off label' in combination with cognitive behavioural therapy. They retrospectively assessed acceptability, feasibility and preliminary outcomes to report initial clinical impressions.

Patients are started on oral naltrexone to establish tolerability before being given the extended-release naltrexone. Most of the cases are managed in their residential facility though they did have some out-patients as well.

The authors' assessment of the cases showed that 10 of the 16 were retained in treatment for at least 4 months and 9 of the 16 had a 'good outcome' which was defined as having a substantially decreased opioid use, improvement in at least one psycho-social domain and no new problems due to substance use.

However, the authors did not include three patients because they never returned for any outpatient follow up after receiving a single dose of naltrexone and only 7 patients continued extended-release naltrexone beyond 4 months.

SMMGP comment: This is described in the literature as a case report and it must be interpreted with all the potential for bias this implies. The exclusion of 3 cases (the ones who didn't come back after one dose) is perfectly acceptable in a case series but highlights the potential problems when it comes to drawing firm conclusions.

The authors suggest that "enthusiasm was particularly strong among patients' parents who embraced the concept of blockade". The authors also noted that some patients were able to overcome the blockade toward the end of the month and it was fairly common for patients to test the blockade. This is quite unsettling – while the authors make a limited attempt to address this it remains a significant concern with naltrexone.

What a case-series is good at doing is promoting debate and as a discussion of the issues around naltrexone this makes for interesting and stimulating reading.

It might be a cliché but this is definitely one area where more research is needed. What we really need is an adequately powered RCT looking at long-term outcomes in a community setting rather than another case-series.

Time to act: a call for comprehensive responses to HIV in people who use drugs.
Beyrer C, Malinowska-Sempruch K, Kamarulzaman A, et al. Lancet 2010; 376:551-63

This paper is the final one of seven in a series about HIV in people who use drugs. The Lancet's coverage has covered all angles:

HIV and risk environments for injecting drug users and prevention of HIV (vol 376 p268-301); treatment and care of injecting drug users, treatment of medical psychiatric, and substance-use co-morbidities (vol 376 p355-387); amphetamine-group substances and human rights (vol 376 p458-485); and finally this paper which opens with this statement:

"The war on drugs has failed. Policies of detention, forced treatment, and incarceration of people who use drugs have been unsuccessful."

These Lancet papers can only be described as comprehensive and are highly recommended for a thorough update on all areas related to HIV and people who use drugs.

Evidence based policy for illicit drugs.
Wood E. BMJ 2010; 340: c3374

The BMJ has carried an issue with the front-cover "Drug users and HIV; treat don't punish". Methadone maintenance treatment significantly reduces heroin use compared with other treatment and it is on the list of the World Health Organization's essential medicines. The Kimber paper (discussed above) in the same BMJ issue adds to the "extensive evidence base for using methadone as a first line treatment for opioid addiction".

SMMGP comment: The lengthy series on HIV and drug users in the Lancet coincided with the BMJ's articles on the same topic. Despite the wealth of evidence for opioid substitution treatment there are still parts of the world where it simply is not reaching – Russia, parts of Central Asia and the Commonwealth of Independent States in particular.

Clinicians in the UK also find that best clinical practice is threatened by wider political motives. In these articles the BMJ and the Lancet have both called for the medical and scientific communities to stand together and call for evidence-based approaches to tackle drug-related harms.

Dr Wood suggests in his BMJ editorial that there is "a clear moral and ethical obligation for those who work in the addictions field." We have to be familiar with the evidence and we have to recognise the limitations of any intervention but there is little value in pontificating on the evidence if it is then impossible to implement because political interference has curtailed the options.

All clinicians have to be prepared to stand as advocates to help users get the best treatments available to them.

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